Claim 5 is pending in this application. Claim 5 has been rejected.

Pursuant to the requirements of 37 C.F.R. §1.821-1.825, applicant has amended and submitted herewith: (1) a paper copy of a sequence listing (Exhibit D); (2) a computer diskette containing the sequence listing (Exhibit E); (3) a statement pursuant to 37 C.F.R. §1.825(f) stating that the computer diskette copy of the sequence listing is identical to the paper copy (Exhibit F); and (4) a Verification Summary Report (Exhibit G).

The substitute sequence listing contains SEQ ID NOs: 1-28, where the original SEQ ID NOs: 5-10 of the application have been amended. SEQ ID NOs: 1-4 and 11-28 of the substitute sequence listing are the same as SEQ ID NOs: 1-4 and 11-28 of the original sequence listing. SEQ ID NOs: 5-10 of the substitute sequence listing have been amended to code for the mature protein. The listing does not contain new matter because the substitute sequence listing reflects the sequences presented in TABLE 2 of the original specification on pages 16-17. SEQ ID NO: 5 is the nucleic acid sequence encoding the pertussis toxin. S1 (SEQ ID NO: 6); S2 (SEQ ID NO: 7); S4 (SEQ ID NO: 8); S5 (SEQ ID NO: 9); and S3 (SEQ ID NO: 10) of the substitute sequence listing correspond to sequences found in TABLE 2. As the amendments to the specification were simply made to indicate the appropriate SEQ ID NOs in the substitute sequence listing and their mature proteins (SEQ ID NOs: 6-10), no new matter is introduced by this amendment.

Enclosed herewith is Table 2 which has been enlarged as required by the Examiner and provided herewith as substitute pages 16, 16a, 16b, and 16c (Exhibit C).

PRIORITY OBJECTION

In order to correct priority of the instant application and the parent application, Serial No. 07/311,612 ("'612 application"), applicant has filed a petition to correct the inventorship of the '612 application under 37 C.F.R. §1.182. Please find a copy of the Petition as filed, enclosed herewith (Exhibit A). Applicant believes that the priority for the instant application has been corrected. The instant application is now believed to correctly claim benefit under 35 U.S.C. §120 to the '612 application. Reconsideration and withdrawal of this priority objection is respectfully requested.

SPECIFICATION OBJECTION

The Examiner has objected to Table 2 (pages 16 and 16a) for informalities regarding the quality of font in the Table. Applicant provides herewith substitute pages 16, 16a, 16b, and 16c in order to address the informalities regarding the font in Table 2 (Exhibit C). Reconsideration and withdrawal of this specification objection is respectfully requested.

35 U.S.C. §112 REJECTIONS

The Examiner has rejected claim 5 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner contends that the recitation of amino acid position without reference to a sequence is indefinite. Applicant respectfully traverses the Examiner's grounds of rejection; however, claim 5 has been amended to include the sequence identifier for the S1 subunit, i.e., SEQ ID NO: 6 in order to address the Examiner's concerns. Reconsideration and withdrawal of this §112 rejection is respectfully requested.

35 U.S.C. §102 REJECTIONS

The Examiner has rejected claim 5 under 35 U.S.C. §102(b) as being anticipated by Burnette, et al. (*Science*, 242: 72-74, Oct. 1988). Applicant respectfully disagrees with this ground for rejection.

As previously discussed in the Priority Objection section, priority has been perfected to the '612 application filed February 15, 1989 by correcting the inventorship. Therefore, the Burnette reference does not qualify under §102(b). Applicant respectfully requests reconsideration and withdrawal of this §102(b) rejection.

Enclosed, for the record in this application, is a copy of a declaration executed by applicant indicating that the invention was complete prior to September 1, 1987 (Exhibit B). This invention date is prior to the *Science* publication date of October 7, 1988, thus antedating the reference. In fact, the applicant is one of the contributing authors of the Burnette *Science* publication. For the 35 U.S.C. §102(a) rejection to be proper, the invention must be known or used by others, or patented or described in a printed publication, before the invention by the applicant for patent. The declaration provides a satisfactory showing that

would lead to a reasonable conclusion that the applicant is the inventor of the subject matter disclosed in the *Science* publication and claimed in the application. Reconsideration and withdrawal of this §102(a) rejection is respectfully requested.

Claim 5 has been rejected under 35 U.S.C. §102(e) as being anticipated by the Burnette Patent (US Patent No. 5,773,600). Applicant respectfully disagrees with this rejection.

The present invention was complete prior to September 1, 1987 as evidenced by the enclosed declaration of Witold Cieplak. The enclosed declaration demonstrates that the applicant completed his invention prior to the earliest priority date of the '600 patent to Burnette. Thus, the enclosed declaration is believed to effectively antedate the Burnette Patent. Reconsideration and withdrawal of this §102(e) rejection is respectfully requested.

35 U.S.C. §103 REJECTIONS

Claim 5 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Pizza, et al. (U.S. Patent 5,925,546). Applicant respectfully traverses this rejection. However, in order to expedite prosecution of this application, applicant has amended claim 5 to recite a single amino acid substitution as suggested by the Examiner. Reconsideration and withdrawal of this §103 rejection is respectfully requested.

DOUBLE PATENTING REJECTION

Claim 5 has been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11, 13, and 15-16 of co-pending Application Serial No. 07/542,149. Applicant respectfully traverses this rejection, because the claims of the copending Application Serial No. 07/542,149 have not yet been allowed. Should claims be allowed and issue into a U.S. patent, applicant will consider the advisability of filing a terminal disclaimer at that time.

CONCLUSION

Enclosed please find a) copies of the Petition Pursuant to 37 C.F.R. §1.182 regarding the correction of inventorship, including the 37 C.F.R. §1.131 Declaration by Jerry M. Keith dated December 19, 1991 (Exhibit A); b) Declaration under 37 C.F.R. §1.131 by Witold Cieplak, Jr. and laboratory notebook pages (Exhibit B with attachments as Exhibit 1-5); c) substitution pages of Table 2 (Exhibit C); d) a substitute sequence listing paper version (Exhibit D); e) an electronic version of the substitute sequence listing (Exhibit E); f) a statement pursuant to 37 C.F.R. §1.825(b) stating that the computer diskette copy of the substitute sequence listing is identical to the paper copy (Exhibit F); and g) a Verification Summary Report (Exhibit G).

Finally, as required by 37 C.F.R. §1.121, a marked up version of the replacement claim and paragraphs of the specification is attached with additions indicated by underlining and deletions indicated by brackets.

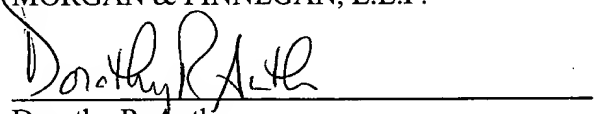
Allowance of the pending claims is respectfully requested. Early and favorable action by the Examiner is earnestly solicited.

AUTHORIZATION

Should any fee(s) be required by the filing of this Amendment and accompanying papers, authorization is hereby given to the Commissioner to charge the amount of any such fee(s) that is/are properly assessable in this application to Deposit Account No. 13-4500, Docket No. 2026-4253US7. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

MORGAN & FINNEGAN, L.L.P.

Dated: March 25, 2003 By: 

Dorothy R. Auth
Registration No. 36,434

Correspondence Address:
MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, NY 10154-0053
(212) 758-4800 Telephone
(212) 751-6849 Facsimile

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please amend and replace the paragraph, at page 24, line 30 through page 25, line 24, as follows:

The amino acid sequence for each subunit was deduced from the nucleotide sequence and is shown in Table 2. The mature proteins contain 234 amino acids for S1 (SEQ ID NO: 6), 199 amino acids for S2 (SEQ ID NO: 7), 110 amino acids for S4 (SEQ ID NO: 8), 100 amino acids for S5 (SEQ ID NO: 9) and 199 amino acids for S3 (SEQ ID NO: 10), in the order of the gene arrangement from the 5-end to the 3-end. Most likely all subunits contain signal peptides, as expected for secretory proteins. The length of the putative signal peptides was estimated after the analyses of the hydrophobicity plot, the predicted secondary structure and application of von Heijne's rule for the prediction of the most probable signal peptide cleavage site. The cleavage site for each subunit is shown in Table 2 by the asterisks. The correct prediction of the cleavage sites for S4 and S1 (unpublished) was confirmed by amino terminal sequencing of the purified mature subunits. The length of the signal peptides varies from 34 residues for S1, 28 residues for S3, and 27 residues for S2, to 21 residues for S4, and 20 residues for S5. All of the signal peptides contain a positively-charged amino terminal region of variable length, followed by a sequence of hydrophobic amino acids, usually in -helical or partially -helical, partially -pleated conformation. A less hydrophobic carboxy-terminal region follows, usually ending in -turn conformation at the signal peptide cleavage site. All subunits except S5 follow the -1, -3, rule, which positions the cleavage site after Ala-X-Ala. The amino-terminal charge for the subunit signal peptides varies between +4 for S1 and +1 for S4 and S5. All described properties correspond very well to the general properties for bacterial signal peptides.

IN THE CLAIMS

5. (amended) A method of producing a polypeptide, said polypeptide comprising at least a portion of mature S1 subunit of *B.pertussis* toxin, including position 9 of the mature S1 subunit of SEQ ID NO: 6, which exhibits substantially reduced ADP ribosyltransferase activity compared to wild-type *B.pertussis* toxin, wherein said polypeptide comprises an

epitope reactive with a protective antibody against *B.pertussis* toxin and comprises [an]a single amino acid substitution other than arginine at position 9 of said mature S1 subunit of *B.pertussis* toxin [other than arginine], said method comprising the steps of:

- expressing the polypeptide from DNA encoding the polypeptide; and
- isolating the polypeptide.